UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

2015-1200

INDUSTRIAL TECHNOLOGY RESEARCH INSTITUTE,

Appellant,

v.

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,

Appellee.

Appeal from the United States Patent and Trademark Office,
Patent Trial and Appeal Board in Interference No. 105,970

APPELLEE'S BRIEF

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CERTIFICATE OF INTEREST

Industrial Technology Research Institute v. Pacific Biosciences of California, Inc.

2015-1200

Counsel for Petitioner-Appellee certify the following:

1. **The full name of every party or amicus represented by me is:**

Pacific Biosciences of California, Inc.

2. **The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:**

Pacific Biosciences of California, Inc.

3. **All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:**

No parent corporation or publicly held corporation owns 10% or more of Pacific Biosciences' stock.

4. **The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or are expected to appear in this court are:**

Weil, Gotshal & Manges LLP – Edward R. Reines, Derek C. Walter, Michele A. Gauger

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TABLE OF CONTENTS

Page(s)

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES

TABLE OF ABBREVIATIONS AND CONVENTIONS

ITRI	Industrial Technology Research Institute
PacBio	Pacific Biosciences of California, Inc.
Board	Patent Trial and Appeal Board
’630 patent	U.S. Patent No. 8,486,630
’551 application	Provisional Application No. 61/201,551
SMRT	Single-Molecule Real Time
CPLM	Circular Pair-Locked Molecule
’970 Interference	Interference No. 105,970
’673 application	Patent Application No. 13/633,673
’178 application	Patent Application No. 13/930,178
’313 provisional	Provisional Application No. 61/167,313
’375 patent	U.S. Patent No. 8,153,375
Personal Genomes	2008 PacBio presentation at Cold Springs Harbor
’614 patent	U.S. Patent No. 7,399,614

STATEMENT OF RELATED CASES

No other appeal in or from this action was previously before this or any other appellate court. Counsel for PacBio knows of no other case pending in this Court or any other court that may directly affect, or be directly affected by, the Court's decision in this appeal.

PRELIMINARY STATEMENT

The Board correctly found that PacBio's prior innovations block ITRI on all fronts.

First, PacBio's SMRTbell™ technology for DNA sequencing renders ITRI's '630 patent invalid as obvious. The alleged point of novelty of the '630 patent, as confirmed in the documents to which ITRI claims priority, is a circular pair locked DNA sequencing template. ITRI concedes, however, that this DNA template is structurally and functionally identical to the SMRTbell™ template that PacBio had developed years earlier.

The only additional concept in the claims of the '630 patent relates to predictable and well-known techniques for the detection of modified bases, including bisulfite and photochemical treatment of DNA. The '630 patent itself acknowledges the prior art status of these techniques, and ITRI confirmed this status during the motion phase through binding admissions. Neither before the

Board nor on appeal did ITRI argue that the skilled artisan would not have combined these well-known techniques with PacBio's SMRTbell™ template or that such a person would not have had a reasonable expectation of successfully doing so. Nor did ITRI present any evidence of secondary considerations.

Second, PacBio's '551 application establishes that PacBio scientists possessed an embodiment of the interference count well before ITRI's earliest possible priority date. As the Board correctly found—and as ITRI cannot reasonably dispute—PacBio's '551 application discloses (1) a CPLM DNA sequencing template, (2) the use of bisulfite treatment, and (3) the comparison of forward and reverse strands of the CPLM for identification of modified bases. PacBio's disclosure firmly conveys to the skilled artisan that PacBio's inventors were in possession of the only step of the interference count that ITRI disputes. Thus, even if ITRI's claims were not obvious, PacBio's prior work presents yet an additional preclusive layer blocking ITRI from seeking a priority judgment in further interference proceedings.

In these circumstances, ITRI attempts to characterize its alleged invention narrowly in the hopes of slipping through some crack in the wall of prior art PacBio presented. ITRI's theory is that the heart of the alleged invention of the '630 patent is the use of "mismatches" to identify modified bases.

ITRI's mismatch narrative, however, is meritless and suffers from fundamental defects. Most important, for the embodiment of the '630 patent that ITRI relies on almost exclusively—the treatment of a CPLM with bisulfite—the specification makes clear that the alleged invention relies on "agreement" to identify modified (*e.g.*, methylated) bases:

> As ^{m}C residues would not be changed by conversion of C to U, the positions where the reads are in ***agreement*** in showing C at a position and/or G as its complement indicate that ^{m}C was present at this position in the original sample.

A97(26:18-22).[1] Given that the preferred embodiment of ITRI's '630 patent does not even require the use of a mismatch to detect a modified base, ITRI's contention that this is somehow a novelty-conferring stroke of genius lacks credibility. ITRI's mismatch theory is nothing more than a litigation artifice presented in an attempt to avoid PacBio's prior art. Because ITRI's only theory is unsupported, ITRI's appeal fails.

Even if it were supported, ITRI's mismatch theory would not allow ITRI to elude PacBio's prior art. While the Board did not adopt ITRI's mismatch theory, it nonetheless found based on substantial evidence—including the disclosure of the references, ITRI's admissions, and expert witness testimony—that PacBio's prior art expressly disclosed the use of mismatches to identify modified bases. Thus, all roads lead to the failure of ITRI's appeal.

[1] Emphasis supplied unless otherwise noted.

Against this backdrop, ITRI uses this appeal to try to take a parting shot at PacBio. Specifically, ITRI seeks to have PacBio's claims held invalid because the Board ruled that ITRI's identical interfering claims were invalid as obvious. According to ITRI, if its claims go down, so too must PacBio's. This position is meritless too. PacBio rebutted any presumption of cross-applicability by explaining that the prior art it relied upon was its ***own*** prior art and thus by statute does not preclude patentability. *See* 35 U.S.C. § 103(c).

The Board's analysis is correct and supported by substantial evidence. The decision should be affirmed.

ISSUES PRESENTED

1. Whether substantial evidence supports the Board's determination that claims 1-28 of the '630 patent are invalid as obvious.

2. Whether substantial evidence supports the Board's determination that the specification of the '551 application establishes that the inventors were in possession of a single embodiment of the count.

3. Whether the Board's decision not to presume that PacBio's '375 patent precluded the patentability of PacBio's own subsequent inventions was supported by substantial evidence demonstrating the applicability of 35 U.S.C. § 103(c).

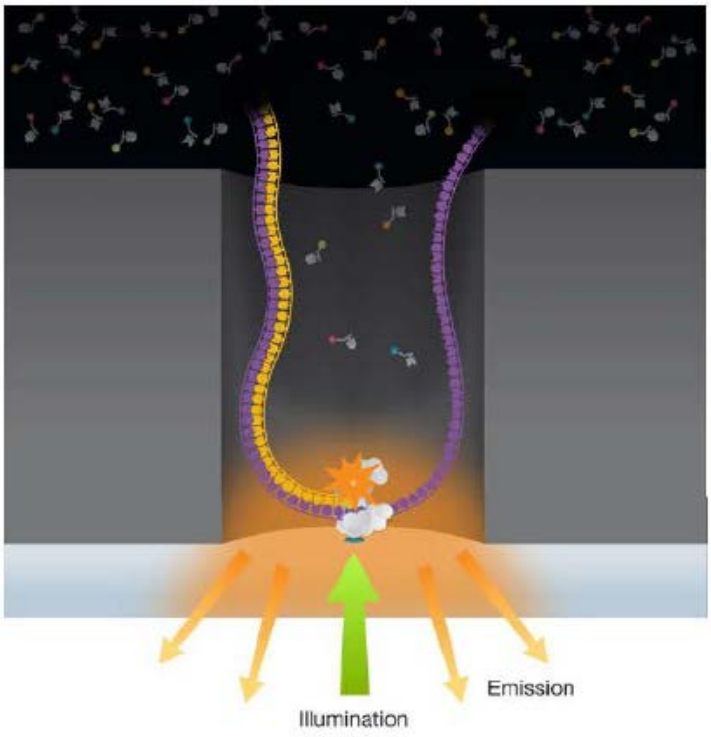
STATEMENT OF THE CASE

I. PacBio's Prior Innovations

A. PacBio's SMRT® Sequencing System

Since its founding, PacBio's business has been the development of new and improved ways of sequencing and analyzing nucleic acids. PacBio's SMRT® ("Single-Molecule Real Time") sequencing product was developed through PacBio's research efforts. As documented below, there is no other sequencing system on the market that operates similarly to SMRT® sequencing or that offers the same capabilities and features.

The SMRT® sequencing system is a sequencing-by-synthesis method in which a single DNA template molecule is contacted with a single DNA polymerase enzyme that is anchored to the surface of a very small volume. A945; A949[Personal Genomes]; A2156[Korlach et al., *PNAS* 2008]. To determine the sequence, the fluorescence given off during incorporation of individually labeled nucleotides by a single polymerase into a single DNA template is monitored by focusing excitation illumination into the bottom of a tiny cavity:



A945[Personal Genomes]; *see also* A2170[Eid et al., *Science* 2009] ("A single molecule of DNA template-bound Φ_{29} DNA polymerase is immobilized at the bottom of a ZMW, which is illuminated from below by laser light. The ZMW nanostructure provides excitation confinement in the zeptoliter (10^{-21} liter) regime, enabling detection of individual phospholinked nucleotide substrates…as they are incorporated into the DNA strand….").

This fluorescence is continuously monitored in real-time. In this way, SMRT® sequencing is a departure from prior art sequencing-by-synthesis methods, in which the sequencing reaction is stopped after every nucleotide incorporation to determine the type of nucleotide that was added to the DNA template (*i.e.*, whether it was A, G, T, or C). *See generally* A705-6['375

patent](5:56-7:56). Because the sequencing reaction is never stopped, SMRT® sequencing has been described as "ultra-fast." A2178[Shendure and Li, *Nature Biotechnology* 2008]. Likewise, because the sequencing reaction proceeds naturally, SMRT® sequencing allows one to sequence much longer stretches of DNA as compared to the prior art. *Id.*

As in all commercially available sequencing-by-synthesis methods, to prevent signal degradation or enzyme inhibition, the labels on incorporated nucleotides must be removed before subsequent nucleotides are incorporated. Prior art sequencing systems commonly use base-linked nucleotides, in which a chemical reaction is used after every base incorporation event to remove the label. *See, e.g.*, A2170[Eid et al., *Science* 2009] ("Other DNA sequencing approaches have used base linked fluorescent nucleotides….These cannot be used in real time sequencing because they are poorly incorporated in consecutive positions by DNA polymerase.").

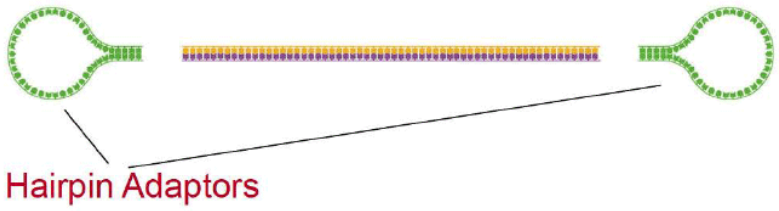
Because PacBio's system operates in real-time with an ongoing sequencing reaction, there is no opportunity to halt the process to remove nucleotide labels. PacBio's solution was to employ a nucleotide in which the fluorophore is linked to the nucleotide in such a way that it is ***automatically*** cleaved by the polymerase at the moment of incorporation. A947[Personal Genomes]. By using this alternative type of nucleotide, PacBio's sequencing system generates a natural DNA strand

containing no fluorophores to either inhibit the polymerase or create background fluorescent signal.

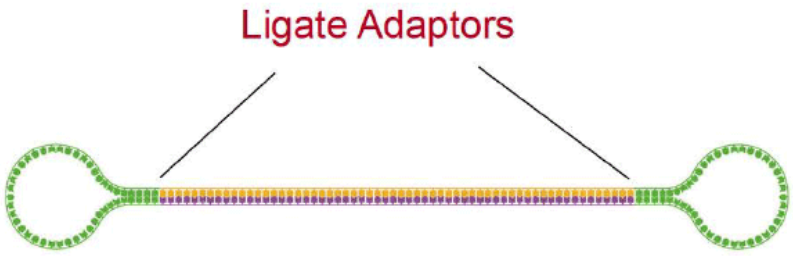
B. The SMRTbell™ Circular Sequencing Template And Its Applications

For use with its SMRT® sequencing product, PacBio developed a versatile new type of DNA sequencing template, referred to as the SMRTbell™ template. The SMRTbell™ sequencing template allows one to sequence both the forward and reverse strands of DNA in a single sequencing run, and further allows for comparison of the sequences of the forward and reverse strands for a variety of purposes. A609-11[’696 provisional]. Among other things, this has allowed PacBio’s technology to achieve an extremely high accuracy rate while also being compatible with single-molecule sequencing.

PacBio achieved this by circularizing a double-stranded fragment of genomic DNA by attaching hairpin adaptors to each end of the double-stranded fragment. *Id.*; A963-70[Personal Genomes]. PacBio’s hairpin adaptors are oligonucleotides with a nucleotide sequence that can partially base-pair onto itself, forming a partially double-stranded stem-loop structure:



A966[Personal Genomes]. The double-stranded ends of the hairpin adaptors are ligated onto the ends of the double-stranded DNA fragment to be sequenced:



A967[Personal Genomes]. Ligating the hairpin adaptors to the double-stranded DNA fragment creates a circular DNA template.[2]

PacBio's SMRT® sequencing system utilizes a polymerase enzyme that can proceed around the template nucleotide by nucleotide until the polymerase either "falls" off of the template or no longer has activity. When a long-lived polymerase is used on a template of reasonable length, the polymerase can proceed all the way around the template, sometimes multiple times, thus gathering sequence information from both the forward and reverse strands in a single sequencing reaction. A969[Personal Genomes].

The portion of a single sequencing read corresponding to the forward strand of the DNA template may be compared to the portion of the same read corresponding to the reverse strand. A610['696 provisional]. Because of the

[2] Due to its characteristic shape resembling a dumbbell, PacBio called its circularized template a "SMRTbell™."

predictable nature of DNA base-pairing—in which adenine in the forward strand of DNA is expected to base-pair with thymine in the reverse strand (and vice versa), and guanine in the forward strand of DNA is expected to base-pair with cytosine in the reverse strand (and vice versa)—having sequenced both the sense and antisense strands provides "a measure of consensus" in that the sequence of the sense strand should correspond largely, according to the base-pairing stated above, to the sequence of the antisense strand. *Id.*; *see also* A611['696 provisional] ("Thus, sequence redundancy comes from both the determination of complementary sequences A and A', and the repeated sequencing of each segment."). This manner of increasing accuracy is often referred to as consensus sequencing.

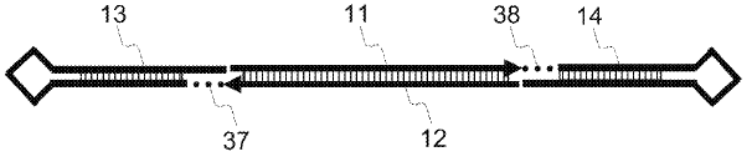
Other applications of the SMRTbell™ sequencing template include the detection of modified bases through a variety of means. In December 2008, PacBio described this in its '551 provisional patent application filing. The '551 application describes not just kinetic methods of detecting modified bases using a SRMTbell™ template, but also methods based on the well-known technique of bisulfite-treatment of DNA. In this method, one treats DNA with bisulfite, and detects methylated cytosine bases by virtue of the fact that the bisulfite treatment leaves them untouched but converts unmethylated cytosine bases to uracil. A918-19 ¶ 17. The '551 application states that the claimed invention contemplates "the detection of uracil in a template nucleic acid" thereby facilitating direct detection

of a modified base. *See, e.g.*, A920 ¶ 23 ("Also contemplated is the detection of uracil in a template nucleic acid. Uracil can be found in DNA as the result of mutagenic agents or as the result of bisulfite-conversion of cytosine in a common protocol used to discriminate methylated cytosine through DNA sequencing.").

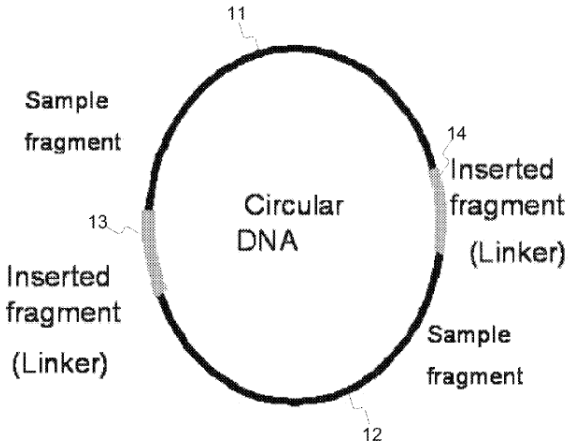
II. ITRI'S '630 Patent

In November 5, 2009—over eighteen months after PacBio filed its first provisional application disclosing the SMRTbell™ template—ITRI filed the application that ultimately issued as the '630 patent. This application essentially replicates PacBio's earlier applications directed to the SMRTbell™ template.

Each and every claim of the '630 patent is directed to methods of determining the sequence of a double-stranded nucleic acid and a position of at least one modified base in the sequence requiring the generation and use of a circular pair-locked molecule ("CPLM"). The '630 patent specification describes a CPLM as follows: "A double stranded molecule containing a forward strand **11** and reverse strand **12** can be combined with inserts that form hairpins **13** and **14**, which may be identical or non-identical, to form a circular pair locked molecule." A87(5:41-45). The '630 specification depicts a CPLM as follows:



A70. Once circularized, a CPLM has the following structure, where the "inserted fragment (linker)s" are hairpins:



Id. The CPLM that is a key element of each claim of the '630 patent is thus structurally identical to PacBio's SMRTbell™ sequencing template.

The '630 patent further describes applications of the CPLM. Just like PacBio's SMRTbell™ template, the CPLM of the '630 patent is described as being useful for consensus sequencing. An entire section of the '630 patent is directed to use of the CPLM for this purpose. *See* A94-95(20:32-22:8). As the '630 patent explains, when "the accepted sequence set contains only two, or at least three, accepted repeats, the sequence of the nucleic acid sample can be determined to be the consensus sequence (see below) of the accepted repeats." A94(20:43-46).

Likewise, a portion of the specification is directed to the detection of modified bases using a CPLM. *See* A95-96(22:63-24:11). Like PacBio's earlier '551 application, a principal embodiment of this approach is based on bisulfite

treatment of the CPLM. A88(8:15-47). As the ’630 patent explains, bisulfite conversion on a DNA template would convert unmethylated cytosine residues to uracil, but would leave methylated cytosine residues unaffected. *Id.* Thus, the ’630 patent states that methylated bases are detected by virtue of the fact that “positions where the reads are in ***agreement*** in showing C at a position and/or G as its complement indicate that ^{m}C was present at this position in the original sample.” A97(26:20-22). The ’630 patent acknowledges that this technique was well-known in the prior art, and cites both the 2004 Laird publication and 2007 Zilberman publication as teaching the technique. A96(23:57-65).

III. The Interference Proceedings

A. Subject Matter and Procedural Overview

This appeal arises from a decision by the Board in the ’970 Interference. The ’970 Interference related to DNA sequencing technology, specifically, the use of well-known techniques for the identification of modified bases (*e.g.*, bisulfite treatment) in connection with a circular sequencing template of the type developed at PacBio (*i.e.*, a SMRTbell™ template).

The Board declared the ’970 Interference on October 29, 2013 between PacBio’s’673 application and ITRI’s ’630 patent. A111-14. On January 14, 2014, the Board granted ITRI’s motion to add PacBio’s ’178 application to the interference. A250-52. PacBio’s ’673 application was afforded the benefit of the

'551 application filed on December 11, 2008. A115. ITRI's '630 patent was afforded the benefit of the '313 provisional, which was filed roughly five months later. *Id.* The Board thus named PacBio the senior party. A110.

The sole count in question in the '970 Interference is claim 24 of ITRI's '630 patent:

> A method of determining a sequence of a double-stranded nucleic acid sample and a position of at least one modified base in the sequence, comprising:
>
> (a) locking the forward and reverse strands of the nucleic acid sample together to form a circular pair-locked molecule;
>
> (b) obtaining sequence data of the circular pair-locked molecule via single molecule sequencing, wherein sequence data comprises sequences of the forward and reverse strands of the circular pair-locked molecule; and
>
> (c) determining the sequence of the double stranded nucleic acid sample and the position of the at least one modified base in the sequence of the double stranded nucleic acid sample by comparing the sequences of the forward and reverse strands of the circular pair-locked molecule, wherein at least one modified base in the double stranded nucleic sample is paired with a base having a base pairing specificity different from its preferred partner base.

A8. Briefly, the count refers to preparing a CPLM template (step (a)), obtaining sequence data of the forward and reverse strands of the CPLM (step (b)), and then identifying the sequence of a CPLM and the position of a modified base by comparing the forward and reverse strands (step (c)). As discussed below, there is no requirement in the count for the modified base whose position is determined to

be mismatched from its preferred partner base. The only element of the count in dispute is step (c). ITRI has never disputed that both PacBio's '375 patent and '551 application disclose all other aspects of the count.

The '970 Interference did not progress past the motion phase. The Board ruled on two motions relevant to this appeal:

- PacBio Motion 2 – Motion for Judgement Based on Invalidity under 35 U.S.C. § 103. A253–82.
- ITRI Motion 2 – Motion to Change Benefit Accorded for Contested Subject Matter. A1025–54.

At issue in PacBio Motion 2 was whether claims 1-28 of the '630 patent are invalid as obvious under a combination of references, the principal reference being PacBio's '375 patent. A258-269. In opposition, ITRI alleged that PacBio had failed to show that the '375 patent was not prior art to PacBio's own involved claims pursuant to 35 U.S.C. § 103(c). A2419.

At issue in ITRI Motion 2 was whether PacBio's involved claims should be afforded the benefit of the '551 application. A1029. ITRI's motion was based solely on the contention that the '551 application did not sufficiently describe step (c) of the count. A1036–42. ITRI did not dispute that PacBio's '551 application sufficiently described all other steps in the count.

On September 3, 2014, the Board decided both motions in PacBio's favor, thus ending the interference.

B. PacBio's Case

PacBio's case was rooted in disclosures of its own prior innovations. *See supra* pp. 5-11. To establish obviousness of claims 1-26 of the '630 patent, PacBio relied on the combination of the '375 patent or a 2008 PacBio presentation at Cold Springs Harbor ("the Personal Genomes presentation") with either the Laird or Matsumura reference. For claims 27-28, PacBio relied on the combination of the '375 patent or the Personal Genomes presentation with the '614 patent. To show that it was entitled to a priority date before ITRI's earliest priority date, PacBio relied on the '551 application.

PacBio's positions were supported by the testimony of Dr. Gerald Zon, who has done extensive research related to novel methods of DNA sequencing, and has authored over 200 publications. A2303[Zon 5/8/13 Decl.] ¶ 9. Notably, Dr. Zon has four patents related to improvements to bisulfite conversion of DNA for sequence analysis, and eight publications on the sequencing of bisulfite converted DNA. *Id.* ¶ 13. Dr. Zon is listed as the sole inventor of the '614 patent, mentioned above.

1. Claims 1-26: The Combination Of The ’375 Patent With Laird

The primary reference relied upon by the Board in finding the claims obvious to ITRI was PacBio’s ’375 patent.[3] The ’375 patent describes PacBio’s SMRTbell™ sequencing template. For instance, Figure 3B discloses a SMRTbell™ sequencing template and circular sequencing of such a template:

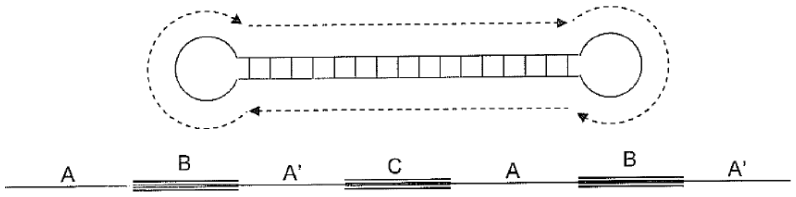


Figure 3B

A689.

The ’375 patent further repeatedly describes comparison of the forward and reverse strands of the SMRTbell™ template. *See, e.g.*, A704(3:12-15) (“The nucleic acid sequence of the sense and antisense strands are then used or compared to determine a consensus nucleic acid sequence of the template nucleic acid.”). It is undisputed that the ’375 patent discloses all steps of claims 1-26 of the ’630 patent, except for steps related to the detection of modified bases.

ITRI did not invent techniques for the detection of modified bases. They were well-known in the art and had been described in many previous patents and

[3] The Board did not rely upon the Personal Genomes presentation. A27 n.27. It also did not rely on Matsumura. It thus found obviousness based solely on the combination of the ’375 patent with Laird.

publications. Here, the Board relied upon the 2004 Laird reference, which is cited in the '630 patent as disclosing the technique of bisulfite treatment for the detection of modified bases. A96(23:57-65). Laird discloses a technique referred to as "hairpin-bisulfite PCR." As Laird explains, "bisulfite conversion… provides information on the methylation state of individual cytosines by converting cytosine (but not 5-methylcytosine) to uracil…." A723. That is, Laird teaches that modified (*i.e.*, methylated) bases can be detected through the use of bisulfite treatment, a point that the parties agree upon. A439 ¶ 111 ("Laird and Matsumura discussed known techniques of converting bases to determine cytosine methylation. **1012**, Abstract; **1013**, Abstract; **2048**, ¶¶ 59, 61. **Pacific Biosciences Response: Admitted.**") (emphasis in original).

2. Claims 27-28: The Combination Of The '375 Patent With the '614 Patent

As ITRI acknowledges, the essential difference between claims 1-26 and claims 27-28 lie in the technique that is used to detect modified bases. While claims 1-26 use comparison of the forward and reverse strands of the DNA template, claims 27-28 use discriminating nucleotide analogs. ITRI.Br.36-37. ITRI did not invent discriminating nucleotide analogs. They had been disclosed long before in the '614 patent:

> A 5-methylcytosine discriminator, which is a deoxyribonucleosidetriphosphate comprising a cytosine-pairing moiety such as a guanosine and a moiety which hinders hydrogen

> bonding between the cytosine-pairing moiety and a 5-methylcytosine is described. The discriminator is able to base pair with a cytosine but not a 5-methylcytosine.

A730. ITRI cannot dispute that discriminating nucleotide analogues were well-known in the prior art, as the ’630 patent itself cites to the ’614 patent for its teaching of this concept. *See* A96(24:41-65).

3. PacBio’s Claim To The Benefit Of The ’551 Application

In the interference, PacBio was awarded the benefit of its ’551 application. It is undisputed that the ’551 application describes steps (a) and (b) of the count. The only dispute is with respect to step (c), which pertains to the detection of the position of a modified base by comparing the forward and reverse strands of a CPLM.

Yet, the ’551 application includes an express disclosure of this concept. While the ’551 application makes clear that the SMRTbell™ template can be used for consensus sequencing and detection of modified bases by kinetic/statistical methods, it also expressly states that it can be used to detect the position and identity of a modified base by comparing forward and reverse strands:

> Such redundant sequence information can provide additional information for discriminating modified from unmodified nucleotides. For example, sequence reads from the sense or “forward” strand can be compared to sequence reads from the antisense or “reverse” strand for the same nucleic acid template to further validate the existence of one or more modified bases in the template nucleic acid.

A918 ¶ 17. The'551 application goes on to describe in the very same paragraph that the described techniques for the detection of modified bases may be carried out using bisulfite-treated DNA. As the '551 application explains, "both A and G would be incorporated at an 'unmethylated' C site (bisulfite-converted to U) while only G would be incorporated at a C site that was not bisulfite-converted to U, e.g., a methylated C site." A918-19 ¶ 17.

C. ITRI's Response To PacBio's Case

ITRI had few responses to PacBio's prior art.

ITRI did not deny that PacBio had conceived of the CPLM long before ITRI, and that this was disclosed in the '375 patent, the Personal Genomes Presentation, and the '551 application. ITRI did not deny that bisulfite sequencing and other methods of detecting modified bases were well-known in the art, and that these methods were, in fact, referenced in its own specification. ITRI did not deny that nucleotide discriminating nucleotide analogs were known. ITRI did not deny that the skilled artisan would have had a reasonable expectation of successfully combining the foregoing techniques, nor did it contend that the combinations would not have been predictable. To the contrary, ITRI agreed with PacBio that the level of skill in the art of the interference count was high. A358 ¶ 79. ITRI produced no evidence of secondary considerations to rebut the prima facie case of obviousness provided by PacBio.

Rather, in an attempt to get around PacBio's prior art, ITRI characterized its alleged invention in a narrow way that it hoped might be perceived as being colorably different from what PacBio had done far earlier. Although acknowledging that the claims needed to be given their broadest reasonable interpretation, ITRI argued that the claims required "using a disagreement between forward and reverse strand sequences of the CPLM to determine the position of a modified base." A333-37.

According to ITRI, it "would be unreasonable to interpret claim 24 as covering a determination of the position of the modified base that does not use the disagreement between the two strands of DNA." A335. ITRI took this position despite the fact that the preferred embodiment of the '630 patent for the detection of modified bases expressly relies on agreement, not disagreement. *See* A97(26:10-22) ("As ^{m}C residues would not be changed by conversion of C to U, the positions where the reads are in ***agreement*** in showing C at a position and/or G as its complement indicate that ^{m}C was present at this position in the original sample.").

All of ITRI's arguments for patentability of the '630 patent over PacBio's prior work assumed the correctness of its theory that the use of "disagreement" was essential to the claimed invention of the '630 patent. ITRI presented no argument for patentability that did not rely on this theory.

Forced into a position where it would be difficult, if not impossible, to defend the validity of its own claims, ITRI attacked the validity of PacBio's claims. Taking a position contrary to 35 U.S.C. § 103(c), ITRI urged that PacBio's co-owned '375 patent was not just invalidating prior art to ITRI's claims, but also the claims of PacBio's interfering applications. A346.

IV. The Board's Final Written Decision

The Board's final written decision determined that ITRI's '630 patent was obvious in view of PacBio's '375 patent (combined with Laird) and that PacBio was entitled to the benefit of the '551 application. A55. These decisions created two independent barriers preventing ITRI from obtaining any further relief in the interference proceedings. At the same time, the Board declined to apply a presumption that PacBio's claims should be invalidated in view of PacBio's co-owned '375 patent.

The Board never found that either the claims of the '630 patent or the count require the use of "mismatches" to identify modified bases. Likewise, the Board did not adopt ITRI's proposed claim construction to this effect. The Board, however, found that the claims of the '630 patent would still have been obvious and that PacBio would still be entitled to the benefit of the '551 application even if ITRI's mismatch theory were correct.

A. The Board's Obviousness Decision

As to obviousness, the Board's final written decision included findings on the factors set forth in *Graham et al. v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). First, The Board made a factual finding as to the level of ordinary skill in the art, concluding that it was a "relatively high level" and that a "person of ordinary skill would have a sophisticated understanding of the molecular biology nucleic acids and their synthesis." A18.

Second, the Board made a factual finding as to the scope and content of the prior art. The Board noted the parties' agreement that "the '375 patent teaches construction of a CPLM and the use of single molecule sequencing to provide redundant sequence information by comparing the forward and reverse strand sequences of the CPLM." A38. As to the detection of modified bases, the Board further found that "Laird teaches that methylated and unmethylated CPG dyads in a bisulfite-treated DNA sequence can be identified by the matching or mismatching of cytosines in the forward and reverse strand sequence data." *Id*. This finding was based on a detailed analysis of the disclosure of Laird. A38-41.

Third, the Board made a factual finding regarding the differences between the claims of the '630 patent and the prior art. In particular, the Board found that there was little, if any difference, between the claimed invention and the combination of the '375 patent and Laird. A38-40; *see* A42 ("The combined cited

prior art references teach or suggest all of the limitation of the claims of the '630 patent…."). The Board rejected ITRI's contention that the '375 patent teaches away from the claimed invention, noting that ITRI had failed to point to any teaching in any reference that would "explicitly or implicitly discourage" the skilled artisan from "looking for base pair disagreements as well as base pair agreements." A40.

Based on the foregoing, the Board concluded that the claims of the '630 patent were obvious. As the Board noted, the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." A42 (citing *KSR Int'l Co. 22 v. Teleflex Inc.*, 550 U.S. 398, 416 (2007)). The finding of obviousness was confirmed by the Board's factual finding that the skilled artisan would be motivated to make the combination to increase the accuracy of discriminating between methylated and non-methylated bases. A42-43.

B. The Board's Decision To Award PacBio The Benefit Of The '551 Application

The Board's analysis was focused on step (c) of the count, which was the sole step in dispute and pertains in part to the comparison of forward and reverse strands of a CPLM to detect the position of at least one modified base. A44-45.

The Board rejected ITRI's arguments that this step was not disclosed in the '551 application. First, the Board noted the high level of skill in the subject matter

of the count. A50. Then, the Board noted the key disclosures of the '551 application. The Board noted that the '551 specification expressly defined "modified bases" to include "methylated bases; bisulfite-converted bases" that "may exhibit different base pairing and/or base stacking properties as compared to native bases." A50-51. It further noted the disclosure in the '551 application explained that "sequence reads from the sense or 'forward' strand can be compared to sequence reads from the antisense or 'reverse' strand for the same nucleic acid template to further validate the existence of one or more modified bases in the template nucleic acid." A51.

Based on these and other disclosures, the Board made a finding of fact that the '551 application describes an embodiment within the scope of the count, even under ITRI's theory that the use of mismatches was required. A52-55.

SUMMARY OF THE ARGUMENT

This appeal presents three issues: (1) whether the claims of the '630 patent are obvious, (2) whether PacBio is entitled to the benefit of its '551 application, and (3) whether, contrary to 35 U.S.C. § 103(c), PacBio's claims should be invalidated based on its own co-owned patent applications.

As to the first two issues, all of ITRI's arguments turn on the correctness of its theory that the count requires using "mismatches" to determine the position of a modified base. This theory, however, is contradicted by the plain language of the

count, the specification of the ’630 patent, the understanding of those skilled in the art as it pertains to bisulfite sequencing, and common sense. The preferred embodiment of the ’630 patent does not even use mismatches, but instead relies on “agreement.” Because ITRI’s mismatch theory fails, and because ITRI presents no arguments that do not assume the correctness of its mismatch theory, ITRI’s appeal fails as well.

Even assuming ITRI’s mismatch theory were correct, reversal still would not be warranted. While the Board never adopted ITRI’s mismatch theory, it nonetheless found that the prior art—including the Laird reference and PacBio’s own earlier-filed ’551 application—discloses the use of mismatches to detect the position of a modified base. This factual finding was supported by substantial evidence and thus cannot be disturbed under the applicable standard of review. This disposes of ITRI’s written description attack on the ’551 application.

It also disposes of ITRI’s attack on the Board’s obviousness finding. This is because ITRI’s arguments rest solely on the contention that the Board’s factual finding regarding the scope and content of the prior art is erroneous, not on any argument that the skilled artisan would not have combined the art or that secondary considerations show non-obviousness. Neither before the Board nor on appeal did ITRI ever point to even a single secondary consideration.

Given the foregoing, ITRI has no plausible path to prevailing in the interference and receiving any valid claims. ITRI's claims are obvious in view of PacBio's '375 patent, and were invented first by PacBio, as demonstrated by the disclosure of PacBio's '551 application.

Seeking to salvage something from its appeal, ITRI urges this Court to invalidate PacBio's claims as well, contending that, if PacBio's '375 patent invalidates the claims of ITRI's '630 patent, it must also invalidate the claims of PacBio's involved applications. However, pursuant to 35 U.S.C. § 103(c), PacBio's prior co-owned patents "shall not preclude patentability" of PacBio's subsequent inventions. While ITRI challenges that PacBio is the actual owner of the '673 and '178 applications, this challenge is dubious on its face and refuted by the submission of obligations of assignment to PacBio from all five of the inventors of the subject matter of the interference count.

ITRI's sole response is to contend that PacBio's proof of co-ownership was inadequate. Although ITRI says PacBio was obligated to confirm ownership by establishing that other individuals are ***not*** inventors (or else submit assignment obligations from the universe of people it suspects ***might*** be inventors), ITRI fails to explain what PacBio should have done to prove the negative that other individuals did not contribute to the conception of the interference count. The

Board's decision not to apply a presumption of cross-applicability was supported by substantial evidence, and this aspect of ITRI's appeal must be rejected as well.

ARGUMENT

I. Standard of Review

A direct appeal of an interference proceeding "under § 141 is based solely on the agency record and reviewed under the standard established by the Administrative Procedure Act." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1296 (Fed. Cir. 2014). Therefore, this Court reviews the Board's factual findings for substantial evidence and its legal conclusions de novo. *Rambus Inc. v. Rea*, 731 F.3d 1248, 1251-52 (Fed. Cir. 2013) (citing *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000)). "A finding is supported by substantial evidence if a reasonable mind might accept the evidence to support the finding." *K/S Himpp v. Hear-Wear Technologies, LLC*, 751 F.3d 1362, 1364 (Fed. Cir. 2014) (citing *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938)). This Court has noted that the "substantial evidence" standard of review for fact findings made by the Board makes the Appellant's burden on appeal "a challenging one." *Leo Pharm. Products, Ltd. v. Rea*, 726 F.3d 1346, 1348 (Fed. Cir. 2013).

For ITRI to prevail on appeal, it "must not only show the existence of error, but also show that the error was in fact harmful because it affected the decision below." *In re Watts*, 354 F.3d 1362, 1369 (Fed. Cir. 2004). The "burden of

showing that an error is harmful normally falls upon the party attacking the agency's determination," which in this case is ITRI. *Shinseki v. Sanders*, 556 U.S. 396, 409 (2009). Even if ITRI were to identify an error in the Board's decision, this Court should nonetheless affirm the Board's decision "on any ground that is supported by the record." *Rexnord Indus., LLC v. Kappos*, 705 F.3d 1347, 1356 (Fed. Cir. 2013).

II. ITRI'S "Mismatch" Theory Is Without Merit

ITRI advances a theory that the heart of '630 patent is the use of "mismatches." *See, e.g.*, ITRI.Br.3 ("ITRI based its innovative method on the insight that ***mismatches*** between the forward and reverse strands of the chemically altered DNA could be used to identify modified bases.") (emphasis in original). All of ITRI's arguments on the two main issues in this appeal are rooted in ITRI's contention that the claims require using a "mismatch" to determine the position of a modified base. In the interference, ITRI even sought to impose a count construction that required this.

ITRI's "mismatch" theory has no basis in the record. This is clear from the claim language alone. Step (c) of the count is as follows:

> (c) determining the sequence of the double stranded nucleic acid sample and the position of the at least one modified base in the sequence of the double stranded nucleic acid sample by comparing the sequences of the forward and reverse strands of the circular pair-locked molecule, wherein at least one modified base in the double stranded nucleic sample is paired

> with a base having a base pairing specificity different from its preferred partner base.

A8. Although one property of the CPLM is that it has a modified base that is "paired with a base having a base pairing specificity different from its preferred partner base," there is no requirement that this be the same base as that used to identify the position of "the at least one modified base." Rather, the only thing that step (c) requires of the "determining" step is that it be done by "comparing the sequences of the forward and reverse strands of the circular pair-locked molecule."

Nevertheless, ITRI asserts that it would be "unreasonable" to interpret this language as "covering a determination of the position of the modified base that does not use the disagreement between the two strands of DNA." A335. In fact, the unreasonable thing would be to limit the claims in the manner ITRI suggests, as this would be contrary to the plain language of the count and therefore not a reasonable interpretation of the count, let alone the broadest reasonable interpretation.

The embodiment of the '630 patent principally relied upon by ITRI—bisulfite treatment of a CPLM—does not even require the position of a mismatch to identify the positions of the modified bases. Rather, the bisulfite treatment converts only ***unmodified*** cytosines to uracil, leaving the modified (*i.e.*, methylated) cytosines unaltered. Thus, as ITRI's '630 patent explains, to identify

the modified bases in this approach, one looks not for "mismatches," but for "***agreement***:"

> In another example, where the circular pair locked molecule has been altered by conversion of C to U, the disagreement indicates that a C was present in the nucleic acid sample at the position occupied by that is a U or T, or is complementary to an A in one read, and is a C or complementary to a G in another read; the logic is that at a position where the sequences disagree, the base which is the product of the conversion reaction, U (which may be read by the sequencing system as a T), has replaced the substrate of the conversion reaction, C, which was present in the nucleic acid sample. ***As ^{m}C residues would not be changed by conversion of C to U, the positions where the reads are in agreement in showing C at a position and/or G as its complement indicate that ^{m}C was present at this position in the original sample.***

A97(26:10-22). ITRI's argument that the detection of this agreement is somehow excluded by the count is therefore contrary to its own specification and the understanding of those skilled in the art. Indeed, in the context of bisulfite sequencing, it is the positions of methylated cytosines that are of interest, *i.e.*, the non-mismatched modified base. A2191[Zon 2d Decl.] ¶ 18.

When one considers this critical embodiment, it becomes clear that the claims were drafted to encompass the detection of both matched and mismatched modified bases, and do not require that mismatches be used to detect the positions of modified bases. In addition to showing that ITRI's proposed count construction is untenable, this embodiment in the specification wipes out any theory that the heart of the '630 patent is "mismatches." Although the specification uses the term

"mismatch" seven times, not once is the term used in connection with the detection of modified bases.

Ultimately, ITRI's theory that the use of mismatches is novel does not even pass the smell test. ITRI's brief argues at length that the identification of modified bases through the use of bisulfite treatment was well-known in the art. *See*, *e.g.*, ITRI.Br.10-11, 14, 52. According, to ITRI's appeal position, the '630 patent's sole distinction over the prior art is that the '630 patent compares against the reverse strand (*i.e.*, the complement) of the DNA being tested whereas the prior art used a so-called "reference sequence" consisting of the original strand being tested. *See* ITRI.Br.14 ("This method differs from the prior art because the prior art did not use a mismatch between forward and reverse strands to locate a modified base. Instead, it compared the sequence of a treated strand to the reference sequence of the untreated version of the same strand….").

This distinction is illusory. Because of the Watson-Crick base-pairing rules, the reverse strand of the DNA that is being tested carries the exact same sequence information and is used in the same manner as ITRI's "reference sequence." There is no meaningful difference between using a "reference sequence" and the reverse strand of the DNA that is being tested. In fact, ITRI's brief describes the concept behind these two allegedly different approaches in exactly the same way:

ITRI's Description Of The Prior Art "Reference Sequence" Approach	**ITRI's Description Of The Claimed Invention**
"Comparing the treated sequence to the reference sequence reveals where conversion occurred because the locations that originally had a C now have a U, and these bases behave differently during sequencing. In contrast, the ^{m}C positions show no change." ITRI.Br.10-11.	"But the bisulfite conversion reaction does not affect 5-methylcytosine (^{m}C). A89[9:1-2]. Thus, bisulfite conversion of a molecule containing both C and ^{m}C alters only C. *See*, *e.g.*, A72[Fig.5B] (illustrating conversion of C but not ^{m}C). Therefore, ^{m}C generally does not occur in mismatches, but U does occur in mismatches when bisulfite conversion is used. For this reason, the term 'mismatched modified base' will generally include U but not ^{m}C." ITRI.Br.14.

ITRI's mismatch theory can only be viewed as a meritless *post hoc* characterization of its alleged invention to attempt to avoid PacBio's prior art. Indeed, when ITRI first submitted the application to which the '630 patent claims priority, ITRI made clear that the point of novelty was the CPLM template, ***not*** the use of a "mismatch" to determine the position of a modified base. The first sentence of the priority document to which ITRI has been given benefit proclaims that this "invention discloses a method for preparing a ***unique*** DNA template that comprises bridging the two complementary strands of DNA fragment together…" A2031[Ex.1003] at 3. Consistent with this, the Board correctly found that the asserted point of novelty of ITRI's alleged invention is not mismatches, but the CPLM itself. A32 ("PacBio asserts that the '375 patent teaches the use of a CPLM

for single molecule sequencing, which ITRI admits in its '313 priority application is the key point of novelty.").

It is undisputed, however, that the CPLM was not developed at ITRI, but at PacBio. This exposes the absence of novelty in ITRI's '630 patent. As documented further below, there is no novelty even if ITRI's "mismatch" theory is assumed correct.

III. The Claims Of The '630 Patent Are Obvious

The first sentence of ITRI's brief is a stern warning about "the dangers of hindsight reasoning." ITRI goes on to assert that the Board fell "prey to hindsight's temptations." ITRI.Br.2.

But, if the Board did improperly fall prey to hindsight's temptations, one would have expected ITRI to rely upon secondary considerations as a check. *See, e.g., Crocs, Inc. v. Int'l Trade Comm'n*, 598 F.3d 1294, 1310 (Fed. Cir. 2010) ("Secondary considerations can be the most probative evidence of non-obviousness in the record, and enables the court to avert the trap of hindsight.") (quotations omitted). ITRI provided no such evidence. Likewise, if hindsight was so evident, one would have expected ITRI to assert that PacBio's combination of prior art would not have been predictable or that the skilled artisan would not have had a reasonable expectation of successfully making the combination. Yet, ITRI never contested these points.

ITRI's silence on these key factual issues is telling, and confirms that there was no improper use of hindsight here. The Board's obviousness finding was correct—a conclusion that is confirmed by an analysis of the evidence presented to the Board at trial.

A. Claims 1-26 Are Obvious

On appeal, ITRI makes the strange and unsupported assertion that the "Board accepted ITRI's claim construction" that required using a mismatch. ITRI.Br.22. In fact, the Board never stated that it was adopting ITRI's proposed claimed construction. ITRI's construction is irreconcilable with the intrinsic record, and the Board could not possibly have adopted it. The very most that can be said is that the Board concluded that the claims would have been obvious ***even if*** ITRI's erroneous construction were adopted.

Nevertheless, all of ITRI's arguments for non-obviousness rely on the false assumption that the claims require the use of a "mismatch" to determine the position of a modified base. ITRI thus tacitly concedes that the claims would be obvious if they are not limited to "mismatches," which, as PacBio explained, is the correct interpretation here. A412-14. Even under ITRI's proposed construction, substantial evidence demonstrates that the prior art discloses the use of a "mismatch" to determine the position of a modified base and that the claims would

still have been obvious. The Board's obviousness finding thus should not be disturbed.

1. ITRI Cannot Dispute Obviousness Under A Proper Interpretation Of The Claims

Substantial and, indeed, overwhelming evidence establishes that the '630 claims are obvious if the claims are not limited to the use of mismatches to detect modified bases.

First, the '375 patent discloses a CPLM and its use for sequencing the forward and reverse strands of double-stranded DNA and then comparing these strands. *See, e.g.*, A688['375 patent] at Fig. 2B; A704['375 patent](3:16-33); A718['375 patent](31:36-32:67). This evidence is undisputed. ITRI has even stated that it "agrees with PBC's statement that the '375 patent and the Personal Genomes presentation taught construction of a CPLM and the use of the CPLM in single molecule sequencing to provide redundant sequence information by comparing the forward and reverse strands." A338:21-25; *see also* A349-50[ITRI Opposition 2] ¶¶ 15-19; A355 ¶¶ 57-60; A350 ¶ 19 ("The '375 patent discloses construction of a cPLM and its use for DNA sequencing. Ex. 1011, e.g., Fig. 2B; col. 3, ll. 16-33; Examples 1-2, cols. 31-32. **ITRI'S Response: admitted.**") (emphasis in original).

Second, ITRI admits that "Laird discloses the use of bisulfite conversion to convert cytosine (but not 5-methylcytosine) to uracil" and that "Matsumura

discloses the use of photochemical transition to convert 5-methylcytosine to (but not unmodified cytosine) to thymine." A351 ¶¶ 24-25. ITRI does not dispute that the use of such techniques for the identification of modified bases were well known in the art. For instance, ITRI's brief summarizes the prior art use of bisulfite conversion for detecting modified bases. *See, e.g.*, ITRI.Br.10-11. The '630 patent itself cites Laird and Matsumura as prior art methods for this purpose. A96(23:49-65).

The only question, then, is whether a skilled artisan would have applied the prior art techniques of bisulfite treatment or photochemical transition for the detection of modified bases to a CPLM template. Substantial evidence confirms that it would have been obvious for the skilled artisan to do so.

First, the parties agree that the level of skill in the art of the '630 patent was high. *See, e.g.*, A358 ¶ 79 ("The relative skill in the art of the Interference Count is high. Ex. 1010, para. 8. **ITRI's Response: admitted.**") (emphasis in original). Consistent with this, the Board correctly found that a skilled artisan would have possessed a "sophisticated understanding of the molecular biology of nucleic acids and their synthesis." A50. This high skill level favors a finding of obviousness. *See, e.g.*, *Innovention Toys, LLC v. MGA Entm't, Inc.*, 637 F.3d 1314, 1323 (Fed. Cir. 2011) ("A less sophisticated level of skill generally favors a determination of

nonobviousness, and thus the patentee, while a higher level of skill favors the reverse.").

Acknowledging the high skill level, ITRI does not dispute that the skilled artisan would have had a reasonable expectation of successfully combining the prior art. Likewise, ITRI does not dispute that the combination would work for the intended purpose of the claims of the '630 patent. Nor does ITRI dispute that the application of bisulfite treatment for identifying modified bases to prior art CPLMs would have simply been the application of a known method to the prior art to yield a predictable result, as PacBio explained during the motion phase. A261-62. For instance, the application of bisulfite treatment to a CPLM would lead to a DNA template in which unmethylated cytosines (but not methylated cytosines) are converted to uracil. The positions of the modified (*i.e.*, methylated) bases can then be read by comparing the forward and reverse strands and identifying the positions where the base-pairing matches the Watson-Crick rules. *See, e.g.*, A2190-91[Zon 2d. Decl.] ¶¶ 14-18. This logic is undisputed.

As PacBio explained, one of skill in the art would have been motivated to compare the forward and reverse strands of a bisulfite-treated CPLM because the '375 patent expressly states that the ability to compare the forward and reverse strands is an advantage of the CPLM. A707['375 patent](9:44-58). Likewise, PacBio explained that "given the well known importance of DNA methylation in

the regulation of gene expression, genomic imprinting and X-chromosome inactivation," one of skill in the art would have been motivated to combine bisulfite treatment with a CPLM template. A262. The Board agreed, finding that "a person of ordinary skill in the art would be motivated to combine the references to increase the accuracy of the invention, particularly with respect to discriminating between methylated and demethylated cytosine bases." A43:1-3. The Board's factual finding regarding motivation to combine is entitled to substantial deference. *See Sibia Neurosciences v. Cadus Pharms.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000) ("Because the jury returned a verdict in favor of SIBIA, we must presume that all factual disputes, such as the motivation to modify, were resolved in its favor").

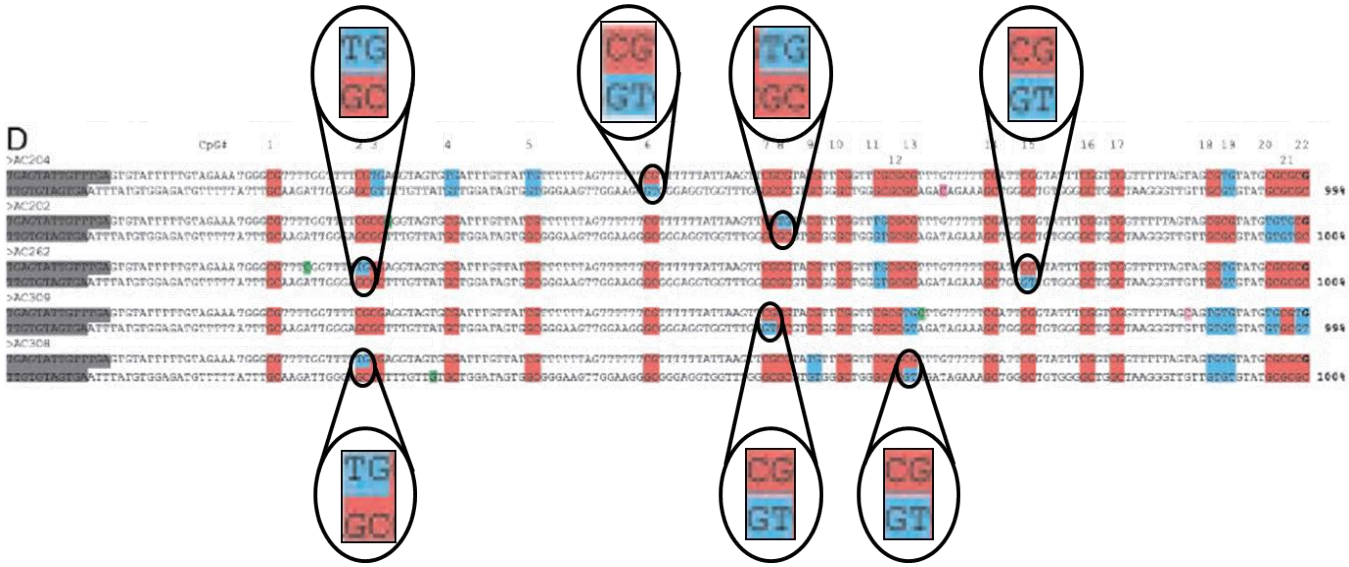
Notably, neither before the Board nor on appeal did ITRI argue that there were any secondary considerations that would rebut the prima facie case of obviousness that PacBio presented.

2. The Claims Are Obvious Even If Interpreted To Require A Mismatch To Determine The Position Of A Modified Base

As noted above, ITRI only attempts to defend validity under an unduly narrow interpretation of the claims that requires the use of a mismatch to detect the position of a modified base. Even assuming ITRI's "mismatch" theory and attendant claim construction had merit, the claims would still be obvious.

ITRI's sole argument for why claims 1-26 would not have been obvious in view of the '375 patent and Laird is that the Board erred in its factual finding that Laird discloses using mismatches to identify modified bases. ITRI.Br.51-53; *see also, e.g.,* A38:23-25[Decision] (the Board finds that "Laird teaches that methylated and unmethylated CPG dyads in a bisulfite-treated DNA sequence can be identified by the matching or mismatching of cytosines in the forward and reverse strand sequence data"). Importantly, ITRI does not dispute that claims 1-26 are obvious if Laird does indeed disclose using mismatches to identify the position of one or more modified bases. Because the Board's factual finding to this effect is supported by substantial evidence, ITRI's appeal of the Board's obviousness determination must be rejected.

First, the Board correctly noted that Laird discloses the use of bisulfite conversion to convert methylated cytosine to uracil. *See* A38-39 (quoting Laird's teaching of bisulfite conversion). The disclosure of this concept in Laird is undisputed. The '630 patent itself relies upon Laird for this concept. A96(23:49-65). Next, the Board correctly noted that Laird compares the forward and reverse strands of bisulfite-treated DNA to identify modified bases using mismatches. A39:18-A40:5. This comparison is evident in Laird, which depicts the forward and reverse strands side-by-side and shows mismatches in the forward and reverse strands through the use of a red/blue highlighting scheme:



A725.[4]

As the Board found, "Figure 2D of Laird is illustrative," and depicts "CpG sequences that have either been transformed to blue-highlighted thymine-guanine pairs (indicating non-methylated cytosine was originally at that locus) and red-highlighted cytosine-guanine pairs (indicating that the unconverted cytosine is 5-methylcytosine at that locus)." A39. As Laird states, "we can distinguish between symmetrical and asymmetrical patterns of methylation for each of the CpG/CpG dyads." A724. That is the mismatches above reveal the existence of hemimethylated regions in which one (but not both) strands of the DNA include a cytosine base that has been modified by methylation. Thus, the mismatches directly reveal the position of a modified (*i.e.*, methylated) base.

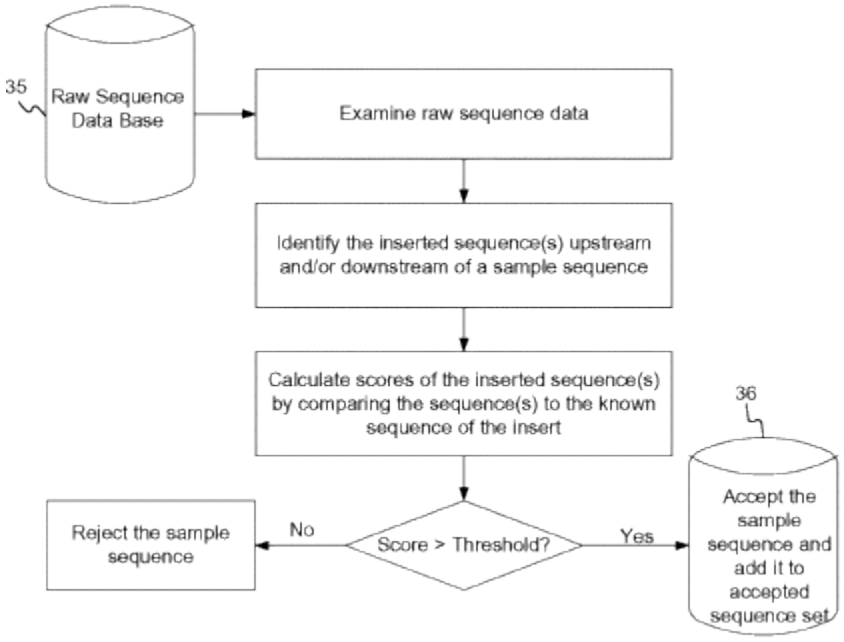
[4] Annotations supplied in black.

This understanding of Laird is confirmed by expert witness testimony. As PacBio's expert explained, "the focus of the Laird paper was on identifying hemimethylated states during DNA replication." A2197 ¶ 32. Citing Figure 2D of Laird, PacBio's expert opined that "Laird directly compared the forward and reverse strands of individual sequencing reads." A2198 ¶ 33; A2200 ¶ 34 (Dr. Zon opines that "Laird actually does compare the forward and reverse strands of a single molecule and thereby identifies a mismatched base (as part of a hemimethylated dyad)"). The blue/red pairings, which include a mismatch, revealed the "assymetrical patterns of methylation." A2198[Zon 2d. Decl.] ¶ 33 ("Asymmetrical patterns of methylation at CpG dyads are depicted by blue/red pairings in the top and bottom strands of the hypermethylated templates in Figure 2D…."). Thus, because the mismatches reveal a hemimethylated region, they reveal the position of a modified (*i.e.*, methylate base).

The Board's factual finding that Laird discloses use of mismatches to identify modified bases is thus based on substantial evidence and cannot be disturbed. Because ITRI's sole challenge to the Board's obviousness determination is that Laird does not disclose the use of mismatches to detect modified bases, *see* ITRI.Br.51-53, ITRI's appeal must be rejected.

3. Claim 23 Of The ’630 Patent Is Obvious

As to claim 23 specifically, ITRI argues that the Board’s obviousness finding was in error because the prior art allegedly does not precisely disclose step (h) of the claim. ITRI.Br.53-55. Step (h) refers to the concept of including within the CPLM “inserts” having a known sequence. The sequence of the insert as determined by the sequencing experiment can be compared against the previously known sequence of the insert, and a “score” can be computed for the insert. A108[’630 patent](47:19-25). The score indicates the quality of the sequencing data and can be used to accept or reject the sample sequence:



A75[’630 patent]. This is nothing more than the age-old concept of using both a variable and a control in an experiment.

This concept is disclosed in PacBio’s ’375 patent:

> Although referred to herein as comparing or assembling the sequence data from multiple reads of a given sequence, and/or from the sense and antisense strands of the sequence, it will be appreciated that any method of assigning a consensus determination to a particular base call from multiple reads of that position of sequence, and/or to a provide an overall consensus sequence for that segment, will be envisioned and encompassed by the term "compare". ***Such methods include actual side-by-side comparisons, scoring methods whereby calls of iterative reads or from complementary sequences are scored by the number of occurrences, and optionally or alternatively additional signal/base calling metrics, to complex algorithms for assigning a base call from multiple indications of the base at a given position***.

A708(11:40-53); *see also id.* at 12:40-59 (describing a model for sequence determination where the input is not "limited to basecalls alone, but can include local or global measures of the individual sequence qualities, sequence context, and characteristic features of the raw signals").

ITRI contends that this disclosure in the '375 patent is inadequate to establish obviousness because it is different than the technique disclosed in the '630 patent. The only difference ITRI identifies, however, is that the control sequence in the '375 patent is not "a ***different*** sequence than the one being accepted or rejected in step (h)." ITRI.Br.54 (emphasis in original). Because the '375 patent does not disclose the exact limitation recited in step (h), ITRI contends, the Board's obviousness determination was erroneous.

This is not the law. Obviousness presupposes differences between the claimed invention and the prior art. What matters for obviousness is whether

"differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103; *Graham*, 383 U.S. at 13. Thus, a claim may still be obvious even if one of its limitations is not is taught in the prior art. *See, e.g.*, *Comaper Corp. v. Antec, Inc.*, 596 F.3d 1343, 1354 (Fed. Cir. 2010) (jury can rightfully find that the claims would have been obvious to a skilled artisan "even if, as Comaper argues, every element in claim 1 of the '955 patent was not present in the AS/400 device"); *Tegal Corp. v. Tokyo Electron Am., Inc.*, 257 F.3d 1331, 1349 (Fed. Cir. 2001) (acknowledging that a claim could be obvious over a single prior art reference that does not disclose one of the limitations in the claim); *PlaSmart, Inc. v. Kappos*, 482 Fed. Appx. 568, 573 (Fed. Cir. 2012) (Board erred by finding nonobviousness based on "minor distinctions between the prior art and the claimed invention").

Here, it is undisputed that the level of skill in the art was high, as the Board held in its order. A18. Although ITRI argues that step (h) was not precisely taught in PacBio's '375 patent, it has never argued that the skilled artisan in the field of the '630 patent would have nonetheless found the differences between the claimed invention and the '375 patent to be so substantial as to render the '630 patent non-obvious. Indeed, ITRI's sole argument to the Board was that obviousness could not be established because the '375 patent did not identically disclose step (h).

A36-37. This argument, however, hinges on the erroneous assumption that PacBio needed to show that step (h) was identically disclosed in the prior art.

ITRI's contention on appeal that the Board's obviousness determination ran afoul of the *Duva* and *Zurko* decisions is unavailing. While "it is impermissible for the Board to base its factual findings on its expertise, rather than on evidence in the record," the "Board's expertise appropriately plays a role in interpreting record evidence." *Brand v. Miller*, 487 F.3d 862, 869 (Fed. Cir. 2007). Here, the Board pointed to the disclosure in the '375 patent regarding the assembly of sequence information from multiple reads and, against the backdrop of the level of skill in the art, determined that the claimed invention was obvious. A41-42. The Board pointed to concrete evidence in the disclosure of the '375 patent in support of its decision, *see* A41, and did not overstep its proper interpretive role in coming to the legal conclusion of obviousness.

B. Claims 27-28 Of The '630 Patent Are Obvious

As to claims 27-28, ITRI's primary argument on appeal is that the Board's obviousness determination must be reversed because the Board's finding that Laird discloses a discriminating nucleotide analog was erroneous. ITRI.Br.55-56.

ITRI ignores, however, that PacBio's obviousness arguments were not based on Laird, but the '614 patent. *See* A268-69. ITRI does not dispute that the '614 patent indeed discloses a discriminating nucleotide analog. ITRI could not

possibly dispute this because the ’630 patent itself relies upon the ’614 patent for discriminating nucleotide analogs. A96(24:41-65). During the motion phase, ITRI even squarely admitted that the ’614 patent discloses discriminating nucleotide analogs for the identification of modified bases. A357 ¶ 76 (“The use of discriminating nucleotide analogs to identify modified bases, including 5-methylcytosine bases, was disclosed in the ’614 patent. Ex. 1002, col. 24, ll. 42-46; Ex. 1014, abstract, claims 1-29. **ITRI’s Response: admitted.**”) (emphasis in original).

Thus, to the extent the Board’s finding that Laird discloses discriminating nucleotide analogs was erroneous, any such error was harmless. This concept—even if not disclosed in Laird—is undisputedly disclosed in the ’614 patent for the purpose of detecting modified bases. While the Board’s obviousness determination was based on Laird, this Court may nonetheless affirm the Board’s decision “on any ground that is supported by the record.” *Rexnord Indus., LLC v. Kappos*, 705 F.3d 1347, 1356 (Fed. Cir. 2013). The record—in particular, ITRI’s binding admissions—supports a finding of obviousness based on the disclosure of the ’375 patent and the ’614 patent.

Pointing to a statement in the PacBio Personal Genomes presentation stating that “Base-Labeled Nucleotides are Problematic,” A946-47, ITRI contends that the prior art teaches away from the claimed invention. ITRI.Br.57-58. According to

ITRI, since the ’614 patent discloses base-labeled nucleotides, and PacBio has allegedly characterized them as “problematic,” one of skill in the art would not combine the ’614 patent with the ’375 patent. *Id.* ITRI’s “teaching away” argument is based on a mischaracterization of the Personal Genomes presentation and a misunderstanding of the law.

The Personal Genomes presentation is a summary of the key features of PacBio’s proprietary SMRT® sequencing system. In this system, DNA is sequenced in real-time. *See, e.g.*, A942-43, A948, A951-54. Unlike other sequencing systems, the sequencing reaction does not stop after each base is added in order to determine the identity of the base that was added. *See generally* A705-6[’375 patent](5:56-7:56). There is thus no opportunity for a separate step in which one removes the labels that are used to identify the bases, which could indeed lead to problems with signal detection and enzyme inhibition. PacBio solves this problem by using nucleotides in which the label is linked to the phosphate, which results in the label being cleaved naturally during the incorporation process. *See* A705[’375 patent](6:24-36); A947; *supra* pp. 7-8.

Thus, when the Personal Genomes presentation states that base-linked nucleotides are “problematic,” it is not teaching that they are undesirable generally. It is simply stating they are not the most appropriate nucleotide for PacBio’s real-time SMRT® sequencing system. ITRI’s contention that PacBio was broadly

asserting that base-linked nucleotides are "problematic," *see* ITRI.Br.57-58, is an inaccurate characterization of the Personal Genomes presentation that ignores context.

Regardless, as PacBio explained, the PacBio SMRT® sequencing platform is not the only platform for which one can use a CPLM. A420:5-22. The '375 patent makes clear that this system is "exemplary," A705(6:58-60), and that a CPLM has "utility across all of the various template directed processes described" therein. A706(8:13-20). This includes classical Sanger sequencing and sequencing-by-synthesis techniques in which base-labeled nucleotides are used because the sequencing reaction is stopped with every base incorporation. *See* A705(5:9-6:23). Thus, a skilled artisan would not be dissuaded from combining the nucleotide discriminating analogues of the '614 patent with the '375 patent.

In fact, even if the only embodiment disclosed in the '375 patent were PacBio's SMRT® sequencing system, the fact that base-linked nucleotides are not the best way to use this system is irrelevant. *See, e.g.*, *In re Etter*, 756 F.2d 852, 859 (Fed. Cir. 1985) (en banc) ("Etter's assertions that Azure cannot be incorporated in Ambrosio are basically irrelevant, the criterion being not whether the references could be physically combined but whether the claimed inventions are rendered obvious by the teachings of the prior art as a whole."); *In re Sneed*, 710 F.2d 1544, 1550 (Fed. Cir. 1983) ("[I]t is not necessary that the inventions of

the references be physically combinable to render obvious the invention under review."); *In re Keller*, 642 F.2d 413, 425 (CCPA 1981) ("The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference….").

IV. PacBio Is Entitled To The Benefit Of The '551 Application

ITRI contends that PacBio is not entitled to the benefit of the '551 application because the '551 application does not describe the use of mismatches to detect modified bases. Thus, just like ITRI's arguments on obviousness, ITRI's arguments on written description hinge on the correctness of its mismatch theory. ITRI presents no argument that PacBio would not be entitled to the benefit of the '551 application if the use of a mismatch to determine the position of a modified base is not a count limitation. Because ITRI's mismatch theory is unsupportable, ITRI effectively concedes that PacBio is entitled to the benefit of the '551 application.

Indeed, ITRI faces a heavy burden in seeking to reverse the Board's decision. "Written description is a question of fact, judged from the perspective of one of ordinary skill in the art as of the relevant filing date." *Falko–Gunter Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006), citing *Vas–Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563–64 (Fed. Cir. 1991). Therefore, so long as the Board's decision was supported by substantial evidence, the Board's findings

cannot be disturbed. *Id.* As documented below, overwhelming evidence confirms that the '551 application discloses an embodiment of the count even under ITRI's narrow interpretation. This is particularly clear when the specification is judged from the perspective of the skilled artisan, as the law requires.

A. Under A Proper Interpretation, PacBio Is Entitled To The Benefit Of Its '551 Application

For the reasons stated above, a proper interpretation of the count does not require that a mismatch be used to identify a modified base. *See supra* pp. 29-34. Rather, all that the count requires is that the CPLM include a mismatched base, and that a modified base be identified by comparison of the forward and reverse strands. Substantial evidence establishes that this is disclosed in the '551 application.

First, as the Board noted, the '551 application is, in part, directed to detection of "modified bases," which are expressly defined in the '551 application to include "methylated bases" and "bisulfite-converted bases." A919['551 application] ¶ 21; A45-46[Decision]. According to the '551 application, in "certain preferred embodiments, detection of a modified nucleotide in a template nucleic acid takes place during a sequencing-by-incorporation reaction in which a polymerase enzyme is synthesizing a nascent nucleic acid strand from the template nucleic acid." A917['551 application] ¶ 16.

Second, as the Board properly found, *see* A45-46, A54-55, the '551 application discloses that detection of the modified nucleotide may be carried out by using comparison of the forward and reverse strands:

> Such redundant sequence information can provide additional information for discriminating modified from unmodified nucleotides. For example, sequence reads from the sense or "forward" strand can be compared to sequence reads from the antisense or "reverse" strand for the same nucleic acid template to further validate the existence of one or more modified bases in the template nucleic acid.

A918['551 application] ¶ 17. The '551 application further makes clear that the described methods could be used in combination with bisulfite sequencing. A920['551 application] ¶ 23; *see also id.* ("Also contemplated is the detection of uracil in a template nucleic acid. Uracil can be found in DNA as the result of mutagenic agents or as the result of bisulfite-conversion of cytosine in a common protocol used to discriminate methylated cytosine through DNA sequencing").

Given this disclosure, ITRI admitted that the templates in the '551 application can include a modified base that is obtained by bisulfite conversion. A2242[Motion 2 Reply] ¶ 116 ("The '551 application discloses that the single molecule sequencing templates of the invention can include a 'modified base' and the modified base can be obtained through bisulfite treatment (uracil) or be a 5-methylcytosine. 1004, ¶¶ [0021], [0023], [0028]. **ITRI's response: admitted.**"). Further, ITRI agrees that such bisulfite-treated templates include a mismatched

base by virtue of the well-known consequences of bisulfite treatment. *See* ITRI.Br.12-13.

Thus, the disclosure in the '551 application of comparing the forward and reverse strands of a mismatch-containing CPLM to identify modified bases could not be clearer. The Board's conclusion that PacBio was entitled to the benefit of the '551 application was thus supported by substantial evidence.

ITRI contends that because paragraph 17 of the '551 application uses the word "validate," it pertains only to the "use of matches to confirm the reliability of sequencing," and asserts that PacBio is relying on inherency for a written description. *See* ITRI.Br.46-47. ITRI admitted, however, that bisulfite treatment was "typically harnessed" to detect modified bases. A2236[Motion 2 Reply] ¶ 85 ("Bisulfite treatment is typically harnessed to detect 5-methylcytosines, which are not mismatched. 1025, ¶ 25. **ITRI's response: admitted.**") (emphasis in original). As the Board properly found, within the context of this typical use of bisulfite treatment, the skilled artisan would not read the '551 application as being directed solely to confirming sequencing reliability. A54:18-21.

On appeal, ITRI's arguments on written description ignore the express disclosure in the '551 application of the use of bisulfite treatment. ITRI's brief reads as if the '551 application includes no such disclosure whatsoever. ITRI.Br.44-51. However, if bisulfite treatment is not being used in the '551

application for the detection of modified bases, then what is it being used for? ITRI never answers this question. ITRI's failure to do so is a tacit admission that the '551 application should not be narrowly read as describing only the use of consensus sequencing to "confirm the reliability of sequencing."

B. PacBio Is Entitled To The Benefit Of The '551 Application Even If The Count Requires A Mismatch To Determine The Position Of A Modifed Base

Although the count does not require using a mismatch to identify the position of a modified base, this concept is nonetheless disclosed in the '551 patent and PacBio would thus be entitled to its benefit even under ITRI's mismatch theory.

There can be no dispute that the '551 application discloses treatment of a CPLM with bisulfite, which converts cytosine to uracil. The resulting uracil bases will then be mismatched with guanine bases in the CPLM. ITRI.Br.13. It is further undisputed that these mismatched uracil bases are "modified bases" as that term is used within the count. A2242[Motion 2 Reply] ¶ 116; A2194[2d. Zon. Decl.] ¶ 24. Importantly, comparison of the sequence of the forward and reverse strands of a bisulfite treated CPLM—which is undisputedly disclosed in the '551 application—will reveal these mismatches. *See, e.g.*, A918 ¶ 17; A920 ¶ 23. And the position of the mismatch is the position of the modified base (*i.e.*, the C that has been converted to U through bisulfite treatment). Thus, even if the count

requires the use of mismatches to reveal the positions of modified bases, this is disclosed in the ’551 application.

ITRI asserts that the disclosure of the ’551 application is inadequate because paragraph 17 of the ’551 application is referring solely to consensus sequencing, which “looks for ***agreements*** (matches) in the sequencing data as an indication of reliability and discards disagreements (mismatches) as errors.” ITRI.Br.24 (emphasis in original). This, however, ignores the disclosure of bisulfite treatment and how this would be understood by the skilled artisan. *Supra* p. 53. The very purpose of bisulfite treatment is to create modified DNA in which cytosine bases are converted to uracil. *See* A2234[ITRI Reply] ¶ 73 (“In a bisulfite treated DNA template, a cytosine is converted to a uracil, and a 5- methylcytosine is not converted. 1002, 23:57-61. **ITRI’s response: admitted.**”).

As the Board found, a skilled artisan that has treated a CPLM with bisulfite would not “discard disagreements (mismatches) as errors,” but would recognize the mismatches as the natural consequence of bisulfite treatment that correspond to modified bases:

> However, given the relatively high level of skill of the average artisan, as we have defined it, it is not reasonable to believe that such a person would not recognize a mismatch occurring between a modified base, i.e., cytosine converted to uracil by bisulfite treatment (as taught by the ’551 application) paired with guanine, and not understand from that mismatch that “at least one modified base in the double-stranded nucleic sample is paired with a base having a base pairing specificity different from its preferred partner base” as

> required by the disputed limitation. ***To reason otherwise, to contend that a person of ordinary skill would only look at "correct" base pair matches and discard, without thought, the mismatched pairs, is not reasonable because the person of ordinary skill would know,* a priori*, that bisulfite-converted uracil would be expected to be paired, incorrectly, with the guanine that would normally be paired with the pre-converted cytosine.*** In other words, a person of ordinary skill would expect to see mismatched uracil-guanine base pairs in a DNA sample strand that had been modified by bisulfite-conversion. Ex. 2026, ¶ [0017]

A54:1-14; *see also* A54:15-A55:2 ("[W]e find that finding a mismatched uracil (or thymine)-guanine pair would 'validate', commonly understood to mean "support or corroborate," the existence of a modified base (i.e., a bisulfite-modified cytosine) in the template nucleic acid on a sound or authoritative basis (*viz.*, knowledge of the bisulfite conversion reaction).").

These factual findings are supported not just by logic, but by substantial record evidence, including the '551 application itself and detailed testimony of PacBio's expert witness explaining the disclosure of the '551 application. *See* A2305, A2309-16[Ex. 1024] ¶¶ 21-24, 40-65. As such, the Board's findings are entitled to substantial deference.

ITRI nonetheless contends that the '551 application "disclaims" the use of mismatches by stating that "the methods herein directly detect the modified base rather than relying on the similarity of uracil to thymine." ITRI.Br.25 (citing A920 ¶ 23). According to ITRI, this alleged "disclaimer" negates the description in the

'551 application of validating the presence of modified bases by comparing forward and reverse strands. *Id.* at 49.

ITRI's argument is illogical. It is true that the '551 application discloses techniques for ***directly*** detecting modified bases that do not rely on the similarly of adenine to thymine, including sophisticated kinetic and statistical techniques. *See, e.g.*, A921-22['551 application] ¶¶ 16, 18, 23, 29. This, however, does not mean the inventors were not also in possession of the technique of the count. They clearly were. This is clear from ¶ 17 of the '551 application, which unambiguously states that "sequence reads from the sense or 'forward' strand can be compared to sequence reads from the antisense or 'reverse' strand for the same nucleic acid template to further validate the existence of one or more modified bases in the template nucleic acid." A918 ¶ 17. "A disclosed embodiment is a disclosed embodiment, no matter the volume of ink required to adequately describe it." *Advanced Fiber Techs. Trust v. J&L Fiber Servs.*, 674 F.3d 1365, 1385 (Fed. Cir. 2012). Likewise, there is no rule that a specification fails because it has multiple embodiments. *See Tobinick v. Olmarker*, 753 F.3d 1220, 1226 (Fed. Cir.2014) (rejecting the argument that "the '205 application does not adequately describe local administration because it mixes local administration techniques with non-local techniques"). There is thus no basis for this Court to disregard the clear disclosure of the '551 application.

V. The ’375 Patent Is Not Prior Art To PacBio’s Involved Claims

ITRI makes a contingent argument on appeal that if this Court holds its claims invalid, then it must also hold PacBio’s involved claims invalid. According to ITRI, the ’375 patent, which is assigned to PacBio, is invalidating prior art against the PacBio claims involved in the interference. ITRI.Br.58. ITRI is wrong, and the procedural history of the interference demonstrates that it would be improper for this Court to invalidate PacBio’s claims.

ITRI’s position is based solely on 37 C.F.R. § 41.207(c), which states that where “a motion for judgment of unpatentability against an opponent’s claim on the basis of prior art is granted, each of the movant’s claims corresponding to the same count as the opponent’s claim will be presumed to be unpatentable in view of the same prior art unless the movant in its motion rebuts this presumption.” *Id.* This regulation, however, expressly allows a movant to rebut any presumption of prior art cross-applicability.

Here, PacBio rebutted the presumption by pointing out that the ’375 patent is not prior art to PacBio under the exemption in 35 U.S.C. § 103(c), which states that subject matter which otherwise qualifies as § 103 prior art “shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.” 35 U.S.C. § 103(c)(1).

The gist of ITRI's argument on appeal is that PacBio did not prove common ownership of the '375 patent and '673 application because PacBio did not adequately establish who the inventors of the '673 application were. *See* ITRI.Br.39-40. This argument is meritless and cannot be adopted given the events of the interference.

Just like any other patent application in which claims are amended or canceled, the inventorship status on the '673 application was in flux during prosecution because the claims were not finalized. Here, the '673 application was filed with 50 original claims and, as ITRI notes, originally listed 11 inventors. However, prior to declaration of the interference, the patent examiner forced PacBio to cancel ***all claims*** except for a single claim that corresponded to the count in the interference. *See* A223-26[12/9/2013 Tr.](17:10-20:2) (PacBio explains that the examiner "made us cancel all of our existing claims other than the single claim that's corresponding to the count…."). The examiner refused to submit the application to the interference specialists at the Patent Office for a declaration of the interference unless PacBio took this action. A2469-70[1/14/2014 Tr.](6:13-7:3). As a result, just prior to declaration of the interference, the claims underwent drastic changes, necessitating a change to the inventorship group.

Accordingly, in the interference, PacBio promptly sought authorization to file a motion to correct inventorship. The Board, however, expressly tabled

inventorship issues for the priority phase of the interference (which was never reached) and did not authorize PacBio's proposed motion. A225-27[12/9/13 Tr.](19:3-21:4); *see also* A202[12/9/2013 Motions Order] ("PBC seeks authorization to move to change its inventorship. The discussion during the telephone hearing suggests that the motion is premature. The motion is NOT AUTHORIZED at this time, but PBC may renew its request if it has a basis that needs to be resolved in this interference.").

Subsequently, when ITRI took the position that PacBio needed to prove inventorship to show common ownership, the Board allowed PacBio to file with its reply brief on obviousness a declaration regarding inventorship, but admonished PacBio that the declaration needed to be very carefully targeted so as to not open new issues. *See* A388[6/2/2014 Tr.](17:9-12) ("So I guess the recommendation or the advice to Pacific Biosciences is make sure you're very carefully targeting what the declaration is addressing and how you're using it in the reply."). Under this specific and narrow authorization from the Board, PacBio submitted a declaration from PacBio employee Stephen Moore authenticating inventor assignment documents.

The Moore declaration authenticated five obligations of assignment to PacBio from all of the proper inventors of the subject matter of the count, thus laying to rest all reasonable doubts about common ownership. *See* A751-52 ¶¶ 3-

4. Although the Board afforded ITRI the opportunity to depose PacBio's declarant, ITRI declined to do so. A2451-52[6/25/14 Tr.](10:16-11:6). Subsequently, when ITRI moved to strike the Moore declaration, the Board denied the motion. A473[Denial of Mtn. to Strike].

On these facts, it is clear that ITRI's appeal on the cross-applicability issue is meritless. Throughout the interference, PacBio took the specific actions authorized by the Board to show common ownership. *See* A2449[6/25/14 Tr.](8:5-13) (counsel for ITRI asserts that PacBio did what the Board "had authorized that they could do"). The Board, upon reviewing the Moore declaration, found the evidence adequate and declined to apply a presumption of cross-applicability. This was not error. Pursuant to the Board's standing order that governs interferences, the Board was free to exercise its discretion with respect to a presumption of cross-applicability:

> Prior art asserted against an opponent's involved claims is presumed to render the movant's involved claims unpatentable as well. Even if the movant does not adequately contest the presumption, however, the Board may exercise its discretion not to hold the movant's claims unpatentable if in deciding the motion the Board determines the presumption is not appropriate.

March 8, 2011, Board of Patent Appeals and Interferences Standing Order ¶ 207, *available* at http://www.uspto.gov/sites/default/files/ip/boards/bpai/interf/forms/standingordermar2011.pdf. Here, a rebuttal was made, the presumption was inappropriate on its face, and the Board properly exercised its discretion in

declining to apply it. Given the procedural history, any other decision would have been unjust.

Notably, while ITRI now argues that ownership necessarily requires PacBio to establish inventorship, ITRI.Br.60, it took a different position in its statements to the Board. In moving to strike the Moore declaration, ITRI argued that while the Board authorized PacBio to submit a declaration supporting its claims of common ownership of the involved PacBio patents and applications, the Board's authorization did not allow PacBio's declaration to address inventorship whatsoever and that, relative to ownership, inventorship was a "new issue." A474[Denial of Mtn. to Strike]; *see also* A454[Doc. No. 157 at 2] (ITRI's statement that it did not raise inventorship in its opposition to PacBio's claims of co-ownership because "there was, after all, no reason to believe it mattered at the time"). ITRI's inconsistent positions as to the relationship between ownership and inventorship belie the weakness of its position, and confirm that this is an empty attack on PacBio's co-ownership of the '551 application.

Indeed, ITRI offers little reason to doubt that the inventorship identification in the Moore declaration is correct. It never bothered to cross-examine Mr. Moore regarding his declaration to develop evidence on this issue despite having been given a chance to do so. ITRI's sole argument is to speculate that some of the original 11 named inventors (including a Stanford University professor) are

inventors who might not have assigned their invention to PacBio. ITRI, however, submits no evidence regarding how the 50 claims in the original patent application compare to the subject matter of the count. Surely, if the claims of the original patent application were so similar to the count such that one would think all 11 of the originally-named inventors must have participated in conception of the count, ITRI would have submitted such evidence. Yet, ITRI is silent.

As ITRI states, the Board did not make factual findings regarding the presumption of cross-applicability. ITRI.Br.59. ITRI thus asks this Court to find cross-applicability and invalidate PacBio's claims in the first instance. This Court should not do so. Because PacBio rebutted any presumption of cross-applicability by submitting the Moore declaration, ITRI cannot show that any alleged error by the Board in failing to make factual findings was not harmless. Nevertheless, if the Court determines otherwise, the Court should not hold that the presumption applies, but should allow the Patent Office to consider the issue as part of further prosecution on PacBio's patent applications. Anything further would be inappropriate given the Board's refusal to authorize PacBio's motion on inventorship from the outset.

CONCLUSION

The Board's decision should be affirmed.

Dated: May 15, 2015

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CERTIFICATE OF COMPLIANCE

The undersigned certifies that this brief complies with the type-volume limitations of Fed. R. App. P. 32(a)(7)(B). This brief contains 13,816 words as calculated by the "Word Count" feature of Microsoft Word 2007, the word processing program used to create it.

The undersigned further certifies that this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6). This brief has been prepared in a proportionally spaced typeface using Microsoft Word 2007 in Times New Roman 14 point font.

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CERTIFICATE OF SERVICE

In accordance with Fed. R. App. P. 25 and Fed. Cir. R. 25, I certify that on this day May 15, 2015, I served the foregoing via the Court's CM/ECF system and electronic mail on the principal attorneys for each party.

Dated: May 15, 2015

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